Department of Genetics
UW, Madison 6, Wis.
Nov. 12, 1953

Dear Alain:

GREETINGS from Esther and Joshua.

If we do not write to you so very often, please do not feel this means we do not think of you, as we recall with warm pleasure the "aimabilities" of the time you spent with us. We have been frightfully busy since mid-Summer, and as time passes, it sometimes seems more difficult to start such a letter only because so many details have accumulated that we want to pass on to you.

I am sorry to learn that your plans at Garches have been disrupted. We do hope you will have a happy station at Pasteur. And, if we do not reach you again in time, let us take the présent opportunity to wish you Joyeux Noel, and ask you to pass the same in due course to Jacques [redacted] and the Novicks and Jacob and Lwoff and the Ephrussis as well.

I am starting this letter at home, and do not recall just when we wrote you last. We had our share of travelling this last year:: I enjoy it now less and less. In February, as we must have recounted earlier, we spent several weeks in a trip to Chamblee, Georgia (together with an Englishman, Clive Spicer, who had been a WHO travelling fellow in our lab) to Edwards'lab. This helped to solidify a continuing collaboration in a study of the immunogenetics of Salmonella-- we have just had a paper in the Journal of Immunology on the synthesis of serotypes, and will of course send this tonyou at the earliest opportunity. You are probably already acquainted with the theme of this particular work, namely that the very numerous naturallyoccurring serological types of Salmonella are but diverse combinations of genetic factors, as can be reconstructed in the laboratory. The biology of transduction in Salmonella, that phage particles can transport fragments of bacterial nuclei, is as fascinating as ever, though we cannot claim to have gotten much more insight into it. However, a variety of different phages have been found to work in Salmonella and we also have a very limited but similar system in E. coli. It will be interesting to see how general a function of viruses genetic transduction turns out to be.

As I said above, we were very busy this summer-- the main reason we declined an invitation to attend the Cold Spring Harbor Symposium and exhaust ourselves still further. However, we did journey to San Francisco, and had an interesting but tiring drive en route. The occasion was a meeting of the Soc. American Bacteriologists, and more particularly the presentation of a "prize" (if you can imagine such a ridiculous thing in Science), but despite all this we enjoyed the opportunity of re-visiting old friends like Tatum and van Niel at their home grounds. We would have been happy to have been able to attend the congresses, in spite of the cost in time, but could not raise the cash for the trip. I had a letter from Ephrussi where he seems to have gott it into his head that there could have been other reasons for our not coming, but he forgets that it is possibly even easier for a European scientist to get a subsidy to visit the US on a brief trip than for any single one of us to the the converse.

As would have been expected, the Salmonella study has been leading us somewhat into immunochemical channels. I do not remember whether I had ever discussed with you the basic facts of phase-variation from a genetic standpoint. It looks as if p.-v. is not an ordinary mutation, as had been once supposed, but an "alternating expression of two genetic potentialities already inhssent in each cell", whatever this means. That is, each diphasic Salmonella has factors at each of two loci, but only one of these is expressed at any time. It turns out that the "specific phase" factors, corresponding to alleles at one of these loci are "chemically" distinguishable from the "group phase" factors, corresponding to the second locus, irrespective of the serological cross-reactions between them. (E.G., eh behaves as phase-1, enx as phase-2).

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The difference was first described by Sertic & Boulgakov (at the d'Herelle laboratory) in 1936, but seems to have been overlooked or discounted since: simply, the phase-1 (specific phase) bacteria are agglutinated not agglutinated by acriflavine, phase-2 is. Unfortunately, other factors can influence dye-agglutination of bacteria, but this result seems to be correct with carefully controlled conditions. A Dr. Aleck Bernstein (an M.D., and Dipl. Bact. from England) is here, officially as a student and Ph.D.-candidate, for a two year fellowship to work this out. He has been extracting the free flagella, and finds that they behave with acriflavine like the bacteria. (In this study we have been finding the Oudin technique to be especially useful!!) We hope tp start some electrophoretic studies to verify whether, as we suspect, the difference in reaction with acriflavine is a reflection of a different ratio of free COOH/NH_2 in the flagellar protein. (Formalin-treated bacteria of either phase become agglutinable, in agreement with this notion). I am hoping that the chemical studies will give us a slightly better insight into the end-effects of phase-variation at a chemical level, and help to plan further experiments on the meaning of the semi-irreversible "differentiation" (in embryological terminology) or narrowing of the initial genetic pluripotencies that seems to be the best description of phase-variation separation.

There has been almost now work to correlate the qualitative receptor analysis of Salmonella in immunochemical terms. Weibull (from Tiselius' laboratory) has been studying flagella, but from a rather different viewpoint. He visited us not long ago, and we were sorry to learn that he is leaving this study to take up another equally interesting-- cytochemical fractionation of bacteria. I did find a paper by K. Meyer in the Ann. Inst. Pasteur, 62:282, 1939, on the inseparability of somatic antigens of Salmonella. Could you help me to find out who this K. Meyer was, and where he might be located at the present time, if possible? (The name and initials are so ubiquitous as to be confusing).

Esther is more or less looking over my shoulder as I write this. We recently moved to a small house, also at the western outskirts of Madison. We feel much less cramped than we did at University Houses (I wish I could say there has been a comparable improvement at the lab!)-- have a lovely, secluded garden-lot which is refreshing even with the approaching winter (though we have had a remarkably warm and pleasant autumn, I should say. No snow yet!) We have also been rearing a pair of black kittens, now almost full grown. At the lab, Esther is still preoccupied with the role of lambda in E. coli heredity (which seems to have been the basis of some recent pronouncements from Lwoff on a new dimension in pathology!). The other people at the lab you probably do not remember. Zinder of course graduated to the Rockefeller Institute last summer. The two girls, Phyllis Fried and Ethelyn Lively have good jobs at Columbia and Illinois. I have two other students now, Larry Morse and Helen Byers, and another post-doctoral associate, Tom Nelson. David Skaar left recently to a job at Cold Spring Harbor (he had been working, somewhat futilely, on E. coli immunogenetics. The material then available was, unfortunately, not very satisfactory. More recently, Esther and Bernstein have picked up some crossable strains of E. coli 055B4, 0111B5, etc., which should be more interesting). Boris Rotman is another post-doct., officially at the Enzyme Institute, but spending half his time here, and working on the activation of E. coli lactase. It would appear that treatment with benzene partially disrupts the cell membranes so that RNA leaks out, but lactase seems to remain behind, though "activated". The activation could conceivably start from the inhibition of lactase by the RNA, but this is perhaps too naive, though being studied carefully, along with several other considerations.

Personally, I have been relaxing temporarily from the transduction studies to work on E. coli cytology, especially for the mating process. This has not yet been seen directly, but we have fairly substantial evidence for the isolation of single zygote cells. These cells later split off the full complement of both parents together with occasional recombinants (in a limited distribution) in concordance with previous data). These results should dispose completely of the idea (that has been

sympathetically entertained by many of your colleagues at the Pasteur') that E. coli recombination involves an intact "gene acceptor" cell, and the transport of small fragments or chromosomes or some unit considerably smaller than the whole nucleus from a "gene donor". But we are not quite ready to publish the details, as I am in the midst of single cell isolations in a rather tedious and long-drawn out way. The cytology unavoidably brings up questions of the microscopic appearance of the nucleus, chromosomes, spindles, etc. There has been a tremendous amount of nonsense on this subject, and even my brief preliminary survey has shown numerous possibilities of artefacts. My own opinion is that the nucleus is typically larger and more vesicular than the usual pictures would show, and that the "granules" usually represented as chromosomes are simply hyperchromatic blobs, possibly segments of chromosomes. There are, however, some very suggestive division stages, like metaphase and anaphase, which may be closer to realities. I have not seen spindles, but have seen numerous granules that could be taken for centrioles by an uncritical observer. But the main objective is the visualization of mating, and we are still perfecting our observational techniques.

I suspect that you have been disturbed at recent political news in this country. Of course, our papers have the habit of playing up McCarthy's charges and then ignoring the belated responses-- as for example Secretary Stevens' announcement that no evidence had been found for recent espionage or loss of documents from Fort Monmouth, and that the dismissals for "security reasons" did not mean that espionage had been found. After making a tremendous fuss, Joe then quietly turned to another question-- he is now fishing at the General Electric works. I wonder if he will ever dare to investigate General Motors! But don't over-estimate the importance of these things. The Democrats made a very impressive showing in the recent by-elections and you can be sure the Republicans are deeply worried (despite the result in California). This Truman-White-Brownell fuss will blow over soon, and is such an obvious political stunt, nothing will come of it. Velde's subpoena was meaningless, and he has been sent to sit in the dunce's chair, you can be sure. All this business is talk, to impress weak and confused minds, and I do not see any serious impairment of our liberties, so long as we fight the intrusions, except in one very important realm-- visas and passports. But I do not recall that Acheson had any more enlightened a policy than is being enforced, more noisily, under the McCarran act. I am sorry that some people have been afraid to stand up for their convictions and retreated behind the 5th Amendment; the best way, in my opinion, to have fought these inquisitions would have been candid testimony. As it is, the refusal to testify cloaks the whole affair (somewhat justifiably) with darkness and suspicion. I wonder if the Inquisitors will have the nerve to compel testimony by passing legislation to bypass the 5th amendment by conferring immunity: I think this would prick their own balloons.

Pogo has recently broken into print again-- we are sending the latest edition.

Could I ask a brief favor, namely to receive advertising lists of French scientific books from Masson and other publishers, as we may wish to order some.

If you have not already heard it, Quin Luttinger has left Madison to take a position at the Department of Physics, University of Michigan, Ann Arbor, Mich. I do not know all of the reasons for his leaving, but he had gotten very deeply involved with a girl (an undergraduate student and leading actress in the Wisconsin Players), and I suspect he was afraid he might be obliged to marry her, not for extrinsic reasons, but owing to the depth of his own attachment, and of this he is of course more fearful than death itself. We had not seen Quin all spring as he had been on leave at Princeton, but curiously enough we met him again at San Francisco. His latest achievment has been the purchase of a tremendous Cadillac convertible car, solid black. I am sorry I have not had much occasion to visit with Ackerknecht or Tucker, and we have scarcely seen the Maison Francais. McShan still haunts the campus.

As ever,